Applicant: Susan L. Lindquist et al. Attorney's Docket No.: 17481-0003001

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Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the

application:

Listing of Claims:

1. (Currently Amended) A yeast cell comprising two integrated copies of an expression

construct comprising a nucleic acid encoding a protein comprising wild-type human alphasynuclein or mutant human alpha-synuclein A53T, wherein the expression construct is integrated

in the genome of the yeast cell, wherein expression of the nucleic acid is regulated by an

inducible promoter, and wherein-induction of production of the protein is toxic to the yeast cell.

2-6. (Cancelled)

7. (Original) The yeast cell of claim 1, wherein the yeast is Saccharomyces cerevisiae,

Saccharomyces uvae, Saccharomyces kluyveri, Schizosaccharomyces pombe, Kluyveromyces

lactis, Hansenula polymorpha, Pichia pastoris, Pichia methanolica, Pichia kluvveri, Yarrowia

lipolytica, Candida sp., Candida utilis, Candida cacaoi, Geotrichum sp., or Geotrichum

fermentans.

8. (Original) The yeast cell of claim 1, wherein the inducible promoter is GAL1-10.

GAL1, GALL, GALS, GPD, ADH, TEF, CYC1, MRP7, MET25, TET, VP16, or VP16-ER.

9. (Original) The yeast cell of claim 1, wherein the expression construct is an integrative

plasmid.

(Original) The yeast cell of claim 9, wherein the integrative plasmid is pRS303,

pRS304, pRS305, or pRS306.

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11. (Original) The yeast cell of claim 1, wherein the protein is a fusion protein comprising a detectable protein.

12. (Original) The yeast cell of claim 11, wherein the detectable protein is a fluorescent

protein, an enzyme, or an epitope.

13. (Currently Amended) The yeast cell of claim 12, wherein the detectable protein is a

fluorescent protein selected from the group consisting of a red fluorescent protein, a green fluorescent protein, a blue fluorescent protein, a, yellow fluorescent protein, and a cyan

fluorescent protein.

14. (Original) The yeast cell of claim 1, wherein at least one gene that encodes a

polypeptide involved in drug efflux or cell permeability is disrupted.

 $15. \ (Original) \ The \ yeast \ cell \ of \ claim \ 14, \ wherein \ the \ at \ least \ one \ gene \ is \ PDR1, \ PDR3,$

or ERG6.

16. (Original) The yeast cell of claim 14, wherein the at least one gene is PDR5.

17. (Previously Presented) A yeast cell comprising two integrated copies of an

expression construct comprising a nucleic acid encoding a protein comprising wild-type human

alpha-synuclein or mutant human alpha-synuclein A53T, wherein the cell expresses a toxicity-

inducing amount of the protein.

18-21. (Cancelled)

22. (Original) The yeast cell of claim 17, wherein the yeast is Saccharomyces cerevisiae,

Saccharomyces uvae, Saccharomyces kluyveri, Schizosaccharomyces pombe, Kluyveromyces

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lactis, Hansenula polymorpha, Pichia pastoris, Pichia methanolica, Pichia kluyveri, Yarrowia lipolytica, Candida sp., Candida utilis, Candida cacaoi, Geotrichum sp., or Geotrichum fermentans.

23. (Withdrawn) A method of identifying a compound that prevents or suppresses alpha-synuclein-induced toxicity, the method comprising:

culturing the yeast cell of claim 1 in the presence of a candidate agent and under conditions that allow for expression of the protein at a level that, in the absence of the candidate agent, is sufficient to induce toxicity in the yeast cell; and

determining whether toxicity in the yeast cell is less in the presence of the candidate agent as compared to in the absence of the candidate agent,

wherein if the toxicity is less in the presence of the candidate agent, then the candidate agent is identified as a compound that prevents or suppresses alpha-synuclein-induced toxicity.

24-26. (Cancelled)

27. (Withdrawn) A method of identifying an extragenic suppressor of alpha-synucleininduced toxicity, the method comprising:

culturing the yeast cell of claim 1, wherein an endogenous gene of the yeast cell has been disrupted, under conditions that allow for expression of the protein at a level that, in the absence of the disruption of the endogenous gene, is sufficient to induce toxicity in the yeast cell; and

determining whether toxicity in the yeast cell is less in the presence of the disruption of the endogenous gene as compared to in the absence of the disruption of the endogenous gene,

wherein if the toxicity is less in the presence of the disruption of the endogenous gene, then the disrupted endogenous gene is identified as an extragenic suppressor of alpha-synucleininduced toxicity.

28-42. (Cancelled).